Prenatal Diagnostics and Obstetrics

Hypertensive disorders of pregnancy

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Summary

Hypertensive disorders complicate about 5-10 % of all pregnancies, but they do account for 15-20 % of maternal mortality and a high amount of maternal morbidity. There are four types of hypertensive disease that include pregnancy-induced hypertension, chronic hypertension, preeclampsia and superimposed preeclampsia. Preeclampsia is a disease with heterogenous etiology. The main pathophysiological mechanism is a disturbed placental implantation and an impaired forming of the spiral arterioles during second trimester. These processes lead to an increased reactivity of the vascular system against vasoactive agents with a generalized vasoconstriction and a dysfunction of the endothelial cell system resulting in activation of coagulation and production of microthrombi. Vascular changes can affect all organs, predominantly the placenta and consequently the fetus, the kidneys and the brain. The likelihood of recurrence during a subsequent pregnancy depends on the etiology, the severity and how early the disease occurred during pregnancy and is between 10 % and 40 %.

The pregnant women and their fetuses have to be under thorough surveillance, if necessary at the hospital because all types of hypertensive disorders can result in a HELLP syndrome or an eclampsia. Severe diseases demand delivery as soon as possible, if possible via vaginal delivery and after treatment for fetal lung maturation, but always taking into consideration further pregnancy complications on the one hand and preterm delivery with a premature infant on the other hand. Intravenous magnesium is the treatment of choice in severe preeclampsia and in eclampsia. Oral antihypertensive therapy for outpatients is only useful in chronic hypertension, α-Methyldopa und β-blocking agents are preferred, for second line therapy dihydralazine or calcium channel blockers such as nifedipine can be used. At blood pressure levels >160/110 mmHg the patients have to be admitted to the hospital and treated with intravenous urapidil, for second line dihydralazine or calcium channel blockers. If a cesarean section is indicated, regional anaesthetic methods should be chosen. As no parameter has been proven to be of prognostic value and there is no effective prophylactic treatment of preeclampsia, management of hypertensive disorders should focus on early diagnosis and adaequate treatment.

Classification

Hypertensive disorders of pregnancy can be divided into four types based on the definitions of 1) Hypertension (RR > 140/90 mmHg) and 2) Proteinuria (> 300 mg/24 h):

- pregnancy-induced hypertension (hypertension after the 20th week of gestation)
- preeclampsia (pregnancy-induced hypertension with proteinuria)
- chronic hypertension (hypertension before the 20th week of gestation)
- superimposed preeclampsia (chronic hypertension with proteinuria) (ACOG 2002)

Pregnancy-induced hypertension (PIH)

PIH is defined as repeated measurements of blood pressure levels of > 140/90 mmHg after the 20th week of pregnancy, without the presence of proteinuria, whereby the blood pressure returns to normal within 12 weeks of delivery.

Preeclampsia

In patients with preeclampsia, repeated blood pressure values of > 140/90 mmHg are measured for the first time during pregnancy and after the 20th week, and are accompanied by proteinuria of > 300 mg/24 h. In addition to hypertension, the presenceof fetal retardation, liver, or kidney disorders, neurological alterations, or anomalies in the blood count, instead of or simultaneously with proteinuria, can lead to diagnosis (Brown et al. 2000).

Chronic Hypertension

Chronic hypertension during pregnancy is present when blood pressure levels are already > 140/90 mmHg before pregnancy or before the 20th week of pregnancy, or when hypertension persists longer than 12 weeks after delivery. Hypertension can be caused by:

- renovascular hypertension (essential hypertension, chronic glomerulonephritis, chronic renal insufficiency, diabetic nephropathy)
- underlying disorders with alterations in the vascular system (diabetes mellitus, the Cushing syndrome, as well as autoimmune disorders such as systemic lupus erythematodes (SLE))
- adipositas

Patients with these preexisting diseases have a predis-position to superimposed preeclampsia.

Superimposed preeclampsia

In superimposed preeclampsia, proteinuria develops during pregnancy in addition to a preexisting hypertension. Both chronic hypertension and proteinuria are present, whereby the proteinuria and blood pressure suddenly i n-crease, or the number of thrombocytes can drop to < 100/nl. The risk of superimposed preeclampsia increases correspondent to the severity of the underlying disease. In very severe cases, the risk can increase to 40 %. In such cases, maternal and fetal morbidity and mortality are higher than in simple preeclampsia or in the underlying disease. Superimposed preeclampsia frequently develops earlier and has a more severe course. This must be taken into consideration during preconceptional counseling of patients with the above-mentioned underlying diseases.

Epidemiology and risk factors

Hypertensive disorders of pregnancy occur in about 5-10 % of all pregnancies, but they are responsible for 15-20 % of all maternal mortalities (Sibai et al. 2005). The placenta is the cause of the patient's disease.

Risk factors for preeclampsia are:

- primipara
- very young or older pregnant women
- essential hypertension
- multiple pregnancies
- African women have a higher risk
- adipositas (the higher the body mass index, the greater the risk)
- diabetes mellitus
- autoimmune disorders (SLE, glomerulonephritis)
- thrombophilia, antiphospholipid antibody syndrome.

Preeclampsia is often found in women with factor V Leiden mutation as well as with variants of the angiotensinogen or methylene tetrafolate reductase gene. Vasospasms in combination with increased vascular reactivity and endothelial cell dysfunction are, as a result, the last common pathway of various pathophysiological mechanisms. A completely different type of etiology would appear to be present in dysfunctional immunotolerance of the embryo or the fetus. There are indications that the risk of preeclampsia, independent of the parity, is inversely proportional to the length and intensity of a couple's sexual relationship before conception (primipaternity theory). On the other hand, studies have shown that the risk of developing preeclampsia in a following pregnancy is influenced less by conception with a new partner, than by the length of time since the previous pregnancy (Skjaerven et al. 2002, amongst others). Paradoxically, smoking during pregnancy decreases the risk of pregnancy-induced hypertension as smoking upregulates the enzyme hemoxygenase-1 (HO-1), which has an antioxidative effect, resulting in a vasoprotective effect. However, women at risk should not be encouraged to smoke.

There is, as yet, no biochemical parameter for predicting preeclampsia before symptoms present. Notching on both sides of the uterine arteries between the 18th and 22nd week of gestation is associated with a significantly increased risk of preeclampsia, but Doppler sonography is not suitable as a screening method, due to its low sensitivity (20 %) and bad positive predictive value (10 %) (Audibert et al. 2005, amongst others). Low-dose administration of acetyl

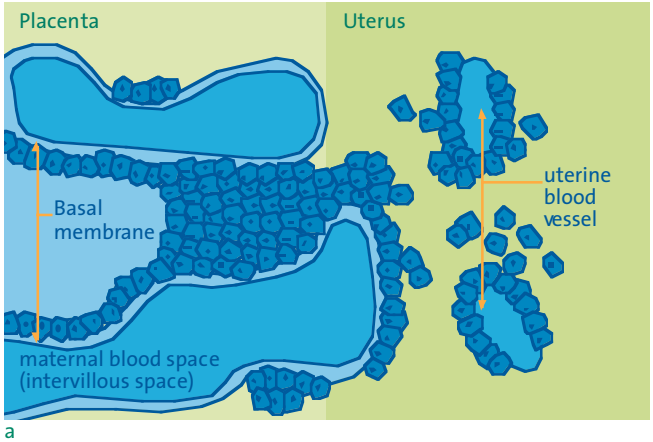
salicyclic acid (100 mg/day) has a mild preventative effect (roughly a 15 % reduction in the risk of developing pre-eclampsia and unfavorable outcome of gestation due to the lower level of thromboxane A2), but only if administered at an early stage (from the 13th week of gestation). Due to associated bleeding complications, we recommend that medication be discontinued at the first sign of symptoms or at the latest, in the 34th week of gestation (Caritis et al. 1998; Coomarasamy et al. 2003; Askie et al. 2007). Today, there are still no known prophylactic measures to prevent preeclampsia. The risk of recurrence is between 10 % and 40 % and it is dependent on when the preeclampsia occurred and on its severity (Hnat et al. 2002). The risk of recurrency is generally greater the earlier the preeclampsia takes place and the more severe it is.

Pathophysiology and etiology

Physiologically, blood pressure falls from the 7th week of gestation, reaches its lowest levels between the 16th and the 20th week and returns to the original levels before pregnancy after the 28th week of gestation (the median blood pressure level in the first trimester is 103/56 mmHg and in the last trimester 109/69 mmHg). This results in about one-third of women with chronic hypertension becoming normotensive in the first half of pregnancy, meaning they can temporarily discontinue hypertensive treatment.

During physiological nidation, the cytotrophoblast invades the uterine spiral arteries and replaces the vascular endothelial cells, the elastic tissue of the media and the smooth muscles. At the beginning of the second trimester, during a second invasion, the spiral arteries remodel to form dilated low-resistance vessels. This remodeling of the uterine spiral arteries ensures adequate blood supply and nourishment of the growing fetus (Merviel et al. 2004).

The pathogenesis of preeclampsia is centered on dysfunctional remodeling of the spiral arteries. Abnormal expression of the adhesion molecule integrin by the cytotrophoblasts leads to an invasion limited to the superficial layers of the decidua. The resulting placental ischemia starts a cascade that leads to systemic alterations in the maternal circulation. Active biological factors are released that damage the endothelial cells and reduce the release of vasodilatatory substances such as NO and prostacyclin (PGI2), whereby the signaling pathways of NO-cGMP and PGI2-cAMP (Fig. 1) become restricted. The placenta factors increase the reactivity to vasoconstrictors such as endothelin, thromboxane, or angiotensin II. This results in intracellular accumulation of calcium, and the calcium-dependent signaling pathways in the smooth muscles increase the activity of vascular protein kinases, such as protein kinase C, whereby the myofilament sensitivity to calcium increases. All of these mechanisms raise the resistance of the vessel and therefore the blood pressure (Tab. 1).



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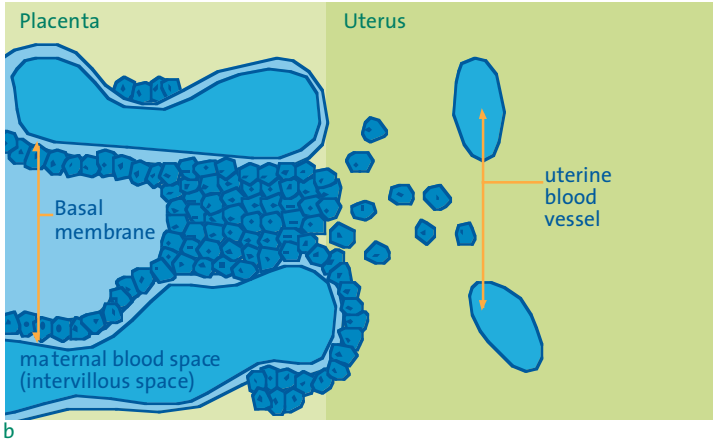

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Fig. 1: Pathophysiology of preeclampsia
a: normal pregnancy
b: preeclampsia due to insufficient trophoblast invasion: damage to endothelial cells → local hypoxia → preeclampsia

Table 1: Alterations to circulation during normal pregnancy and in preeclampsia

Normal pregnancy	Preeclampsia
cardiac output per minute increases	cardiac output per minute increases, remains the same, or decreases
plasma volume increases	plasma volume increases, remains the same, or decreases
reduction of total peripheral resistance	total peripheral resistance increases
arterial blood pressure decreases	arterial blood pressure increases
renal perfusion increases	renal perfusion is reduced
renal vascular resistance is reduced	renal vascular resistance increases
response to vasopressors decreases	response to vasopressors increases
reactivity to vasoconstrictors decreases	reactivity to vasoconstrictors increases significantly

During manifestation of severe preeclampsia, the processes associated with disrupted placentation lead to generalized vasospasms that can affect all vital organs. The interendothelial cell barrier is suspended due to the damaged endothelial cells, making it possible for components of the blood, such as thrombocytes and fibrinogen, to leak out and accumulate in the subendothelial space. These alterations to the vessels and the local hypoxia of the surrounding tissue lead to bleeding, necrosis, and other disorders of the end organs, to the point of accumulation of fibrin deposits. The activation of the coagulation system results in intravascular microangiopathic hemolysis, activation of the thrombocytes, and resulting generalized production of thrombocytes in the capillary system with associated disorders in the microcirculation, which can manifest in many ways from head to foot (see below). In preeclampsia, the lowered total blood volume results from the generalized vasoconstriction and increased vascular permeability. Simply the physiological loss of blood during birth can therefore have fatal hemodynamic consequences.

Changes also take place in the kidneys: during pregnancy, renal blood supply and the glomerular filtration rate (GFR) are physiologically increased. In preeclampsia, however, both of these parameters decrease – so significantly that they can fall below the normal values for non-pregnant women. As the levels of uric acid increase, due to the decrease in glomerular filtration, they are an indicator of the severity of the course of the disease. The creatinine levels also alter: due to the decrease in clearance, the level can rise to > 2 mg/dl. Oliguria is the cardinal symptom. Proteinuria develops when large plasma proteins that are not normally eliminated by the kidneys are filtered due to the increase in permeability, and smaller proteins that are normally filtered are not resorbed due to restricted kidney function. Usually the kidney function recovers completely in women whose kidneys were healthy before delivery; however, if the kidneys were already damaged before pregnancy the impairment is sometimes irreversible.

Clinical picture

PIH and chronic hypertension can occur without symptoms and are sometimes incidental findings during medical checkups. Significantly raised blood pressure values can lead to headaches, dizziness, and nausea. Possible symptoms of serious preeclampsia or the HELLP syndrome are aversion to light, upper abdominal pain or headache, as well as decreasing excretion with severe water retention. The following is a summary of the many-faceted clinical picture of severe preeclampsia:

- RR > 160/110 mmHg
- severe proteinuria > 5 g/h
- oliguria 400 ml/24 h
- thrombocytopenia < 100/nl
- increased aminotransferases (ALT/AST)
- increased creatinine in serum > 0.9 mg/dl
- uric acid level > 7 mg/dl
- pain in the upper abdomen, headaches, visual disorders, nausea, vomiting, flickering of the eyes, hyperreflexia
- fetal retardation

Thrombocytopenia develops due to activation and aggregation of the thrombocytes, and to microangiopathic hemloysis resulting from severe generalized vascular spasms. It occurs in 15 % of patients with preeclampsia with no HELLP syndrome. Delivery should be induced quickly if thrombocytopenia develops or if there is a rapid continual decrease in thrombocytes.

Periportal hemorrhagic necrosis is probably responsible for the high transaminase activity in preeclampsia or the HELLP syndrome. The rise in transaminases is also a result of restricted perfusion of the liver due to generalized vasoconstriction (in areas where circulation can be critical). Necrosis can lead to small subcapsule hematoma. Upper abdominal pain is an expression of the ischemic edema in Glisson's capsule. Therefore, if transaminase levels rise delivery should also be induced rapidly. Headaches are an expression of disruption of the blood supply to the cerebral region, with a resulting loss of cerebral vasoautoregulation. Cerebral symptoms often precede an eclamptic attack. Edemas develop due to water leakage following endothelial lesions. This leads to proteinuria in the kidneys and promotes the development of edema via lowered plasmaoncotic pressure.

Serious preeclampsia can develop into a HELLP syndrome, a particularly severe form of pregnancy-induced hypertensive disorder. The HELLP syndrome is a symptom triad: Hemolysis, increased transaminase values (Elevated Liver enzymes) and thrombocytopenia (Low Platelets«). The mortality rate is about 1 %. The main symptom is pain on the right side of the upper abdomen. The HELLP syndrome develops in 15 % of all pregnant women with preeclampsia or eclampsia; however, preeclampsia must not necessarily precede the HELLP syndrome (15-20 % of patients have an isolated HELLP syndrome).

Due to severe complications (see below), prompt delivery is the preferred treatment. Glucocorticoids can delay the progression of the disorder. It is therefore possible to attempt lung maturity treatment in early pregnancy. Present know-ledge indicates that in general, conservative treatment of the HELLP syndrome is not recommended. In one out of every three cases, the HELLP syndrome does not manifest until confinement. The risk of recurrence of an isolated HELLP syndrome is about 5 %.

Eclampsia is a further serious complication of pregnancy-associated hypertension. Eclampsia is characterized by one or several generalized tonic-clonic seizures. In principle, eve ry pregnant women who undergoes a seizure must be treated for eclamptic seizure until another cause has been determined! Eclampsia occurs to 38 % prepartal, 18 % peripartal and about 44 % postpartal. Cerebral vascular spasms are probably the cause. Eclampsia develops in 1/1 000-2 000 pregnancies, increasing the risk of severe complications, such as Placental abruption or disseminated intravascular coagulation (Zhang et al. 2003) about 25-fold. Prodomi are flickering of the eyes, aversion to light, and/or hyperreflexia. During a seizure, which often lasts over a minute, the diaphragm is fixed and respiration ceases. Often, after a subsequent spontaneous regulation of the breathing, a kind of coma follows. The length of the coma can vary, sometimes lasting until the next seizure. If further attacks follow without the wo men regaining consciousness, the state is termed status eclampticus. Usually the patient experiences retrograde amnesia of the period immediately before and after the attack. If the attack occurs during contractions, it may intensify them. Due to maternal hypoxia caused by the seizure and lactic acidosis, the CTG also frequently alters during contractions, sometimes causing fetal bradycardia. If bradycardia persists, a immediate delivery should be considered. Eclampsia can culminate in fatality. Patients usually die during an attack or shortly afterwards, following massive cerebral bleeding, of which postictal fever is a sign (for complications see below).

Complications of preeclampsia, the HELLP syndrome, or eclamptic seizures (50 000-100 000 mortalities per year worldwide):
- placental abruption
- intrauterine fetal death
- disseminated intravascular coagulation
- cerebral hemorrhages resulting in amaurosis, hemi- or tetraplegia
- left-heart failure
- renal insufficiency
- necrosis of the liver
- myocardial infarction

Management of pregnancy-induced hypertension

The pregnant woman should keep a blood pressure diary. Urine tests for protein should be carried out regularly. The patient should also be counseled on the symptoms of preeclampsia. To exclude any additional negative influences on the vascular system caused by stress, the patient should not physically exert herself and should not work. Oral antihypertensive treatment to keep the blood pressure at a slightly raised level within the normal range (with alpha-methyldopa for instance), has proved unnecessary. Antihypertensive treatment and hence inpatient monitoring is necessary when blood pressure levels of > 160/110 mmHg persist. Fetal growth should be monitored sonographically in all hypertensive disorders of pregnancy at two- to four-weekly intervals in the second half of pregnancy, for early identification of any intrauterine deficiency.

Management of preeclampsia and superimposed preeclampsia

From a pathological point of view, the organ that causes the disease should be removed, i. e. the placenta. This means that in preeclampsia, regardless of the degree, the pregnant woman must be delivered after the 37th week of gestation, i. e. delivery must be induced or, in severe cases, the patient must even undergo elective cesarean section. Besides admission to hospital, lung maturity treatment is indicated before the 34th week of gestation. The primary goal is to ensure the safety of the mother; delivery of a mature child is of secondary importance. Therefore, in severe preeclampsia, if any doubt remains after the completion of lung maturity treatment, delivery should be induced if the risk of prolonging the pregnancy outweighs the advantages, and definitely after the 34th week of gestation. Women with mild preeclampsia can be treated as out patients after initial evaluation of the severity of the disease has taken place in hospital.

The severity of the disease can best be judged by balancing intake and excretion rather than by monitoring the weight. In severe cases, excretion decreases to the extent of an oliguria with urine excretion of < 300 ml/day. The extent of proteinuria can fluctuate during the day; urine should therefore be collected for a 24-hour period. In serious cases protein loss is up to > 3 g/day. The frequency of blood pressure and CTG monitoring is dependent on the patient's clinical picture; continuous surveillance may be required.

Management of chronic hypertension

Hypertensive treatment is indicated for chronic hypertension. In principle, the pregnant woman should continue to take the medication for blood pressure adjustment that has already been prescribed, taking contraindications into consideration (e. g. diuretics and ACE inhibitors, as well as angiotensin receptor antagonists). Alpha-methyldopa is the medication of choice for initial blood pressure adjustment. It lowers peripheral vascular resistance with only minimal reduction of cardiac output. If the blood pressure does not decrease adequately, β-blockers (e. g. metoprolol 50 mg/day or bisoprolol 5mg/day) are the first choice in medication. Calcium channel blockers such as nifedipine (5-30 mg up to 3 x daily) or amlodipine and dihydralazine (starting with 12.5 mg daily, increasing to 100 mg) can be administered orally. Unlike the treatment for chronic hypertension in non-pregnant women, if blood pressure does not fall sufficiently, the dosage of the primary medication should be increased, rather than commencing a combined therapy. These high-risk patients should be counseled thoroughly on the symptoms of preeclampsia and they must be admitted to hospital for surveillance if blood pressure rises > 160/110 mmHg. The following parameters play a role:

- fluid balance
- determination of protein excretion using a 24-hour urine collection test
- periodic RR measurements
- monitoring of creatinine values, the blood count, transaminase values and LDH activity
- fetal monitoring
- no physical exertion, but not absolute bed rest.

Fetal monitoring in hypertensive disorders during pregnancy

PIH alone triples the risk of intrauterine death. In patients with preeclampsia, the risk is even higher (due to insufficient placental perfusion, placental infarction, and placental abruption). Oligohydramnios and commencing fetal retardation are early signs of inadequate intrauterine supply, which can be seen in the head-abdomen ratio. Fetal biometry and Doppler sonography should be carried out about every two weeks in patients with hypertensive disorders during pregnancy, and the pregnant woman should be shown how to check the movements of the fetus. If there is retardation in fetal growth – this is related to preeclampsia in 10-25 % of all cases – the patient must be admitted to hospital for CTG monitoring, lung maturity treatment, and Doppler sonography at least once a week. If the CTG or the Doppler sonography show pathological findings, delivery by cesarean section is indicated for the benefit of the fetus. Before the 34th week of gestation, the advantages of prolonging the pregnancy after completion of lung maturity treatment, with regard to the intrauterine maturation of the fetus, must be weighed against the risk of intrauterine death. If a patient with hypertensive disorder suffers from any acute unclear pain in the lower abdomen or vaginal bleeding, even if there are no relevant accompanying symptoms, placental abruption must always be kept in mind!

Intrapartal management of severe preeclampsia and the HELLP syndrome

The intrapartal management of preeclampsia can be summarized as follows:

- intravenous $MgSO_4$, if necessary with ECG and respiration monitoring
- intravenous urapidile (alternatively dihydralazine)
- continuous CTG monitoring
- volume balance
- vaginal delivery is safest
- if cesarean section is performed, it should preferably be carried out with regional anaesthesia

Closed-meshed monitoring is necessary as severe preeclampsia can develop from the mild form due to alterations in the heart minute volume and the concentrations of stress hormones during contractions. In severe cases, magnesium can be infused intravenously for the prevention of seizures (e. g. 8 mmol/h, equivalent of four ampules $MgSO_4 \times 7\ H_2O$ 20 g/480 ml, 2 g/h). Magnesium halves the risk of eclampsia and reduces maternal mortality

(Witlin u. Sibai 2001; The Magpie Trial Group 2002; Belfort et al. 2003). Therapeutic plasma levels are 4-7 mmol/l. Magnesium passes the blood-brain barrier (and has a stabilizing effect on the membranes of the central nervous system), and is excreted exclusively via the kidneys. As the level rises quickly if there is any renal dysfunction, and concentrations of > 7-10 mmol/l can cause respiratory arrest, the tendon reflexes, urine excretion and breathing rate, or – if possible – plasma levels, should be closely monitored. Magnesium is of no therapeutic use in mild forms of preeclampsia or in PIH (Witlin et al. 1997; Livingston et al. 2003). Alternatively, phenytoin can be used for the prevention of seizures in beginning renal insufficiency starts to develop. If hypertension is severe, blood pressure is adjusted by medication with intravenous urapidil (via a perfusor, starting with 1mg/h, increasing the dose to up to 30 mg/h), or alternatively with dihydralazine (initial dose of 5 mg, then a bolus of 1 mg every 15-20 min). Due to reduced perfusion of the placenta and the fetus, the blood pressure should not be lowered too quickly and always controlled by CTG monitoring. If possible, vaginal delivery is preferable due to the abrupt alteration in volume during cesarean section and great loss of blood, which must be expected if the cervix findings are favorable. If a cesarean section if performed, regional anesthesia should be used instead of intubational narcosis, as with the latter, there is risk of aspiration, and intubation may be unsuccessful due to possible edema in the respiratory tract. Apart from this, cerebral pressure increases considerably during intubation and extubation. With peridural and spinal anesthesia, a drop in blood pressure should be prevented by careful volume support. Regional anesthesia is not possible with thrombocytopenia of < 70/nl.

During a HELLP syndrome with increasing transaminases and falling thrombocyte numbers the focus is on ending the pregnancy. Acute upper abdominal complaints and an isolated HELLP syndrome are often accompanied by a fulminant increase in transaminase and LDH levels. The rapid decrease in thrombocyte values is the result of generalized vasoconstriction. If delivery takes place too late, it is often no longer possible to control the course of the disease and damage to the liver and renal functions and to the central nervous system (amaurosis, coma) threaten. Therefore, the patient should only be treated, with careful monitoring i. e. every three to four hours in emergency labor (does the author mean labor=contractions or emergency laboratory tests?), with corticosteroids, e. g. 2 x 12 betamethasone. This treatment often leads, particularly with the HELLP syndrome on top of severe preeclampsia, to cessation of the pathological dynamics. For this reason, the HELLP syndrome is treated conservatively, particularly in the early weeks of gestation (24th to 28th week).

Management of eclampsia

The medication of choice in eclamptic seizure is intravenous magnesium sulfate 2-6 g, followed by a maintenance dose of 2 g/h; if there are any contraindications, diazepame should be administered, and delivery should be performed or induced in all pregnancies beyond the 34th week of gestation. Vaginal delivery is recommended even after an eclamptic seizure – similar to the situation in severe preeclampsia – as serious morbidity is less rare after vaginal delivery than after cesarean section.

Management during postpartum period

Unlike in gestational diabetes, blood pressure levels do not normalize immediately, even if they are in the normal range immediately postpartal or after a cesarean section (due to loss of blood). Eclampsia or a HELLP syndrome can also develop after delivery (this applies to 30 % of patients for the respective entity); the patient should be kept under intensive surveillance, with monitoring of circulation (RR, fluid balance, O_2 saturations) for at least 48 hours, and magnesium should be administered for the prevention of seizures. Antihypertensive treatment should be continued, and depending on the RR values, should be tapered off when applicable. Primary ablactation is not recommended in general if it is only because of the medication. Persistent hypertensive blood pressure levels with otherwise normal clinical findings are not a reason to prolong hospital stay. If there is increased risk of thrombosis after a cesarean section, or because the patient is bedfast, treatment with low molecule heparin at a prophylactic dosage should be considered (e. g. dalteparin 2 500-5 000 IU/day). If thrombocytopenia is present after a HELLP syndrome, this therapy can only be commenced when thrombocyte numbers return to over 100/nl. The patient is encouraged to measure her own blood pressure after she has been discharged and to continue medication until the blood pressure level has returned to normal.

Urine excretion is a sign of recovery during postpartum period. Proteinuria and edema generally recede after one week, and the blood pressure is nearly always back to normal after two weeks. If the liver and kidneys have been severely damaged, it can be days and weeks, until the original status is regained. Often, the pathological values continue to rise for a short time after delivery , before they finally decrease. Damage to the central nervous system can be irreversible. The longer hypertension persists after delivery , the more likely that it is caused by chronic vascular or renal damage and the less favorable the prognosis of a restitutio ad integrum. Every patient who has suffered hypertensive disorders during pregnancy should contact a nephrologist or cardiologist for treatment. The physician should check the blood pressure and carry out diagnostics for renal function (the worsened condition often persists after alterations during pregnancy that do not manifest before delivery). It should be pointed out to the patient

that there is an associated life-long risk of developing chronic hypertension, and counseling on preventative measures should be provided.

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Keywords

Eclampsia, HELLP syndrome, hypertensive disorders of the pregnancy, preeclampsia, pregnancy-induced hypertension

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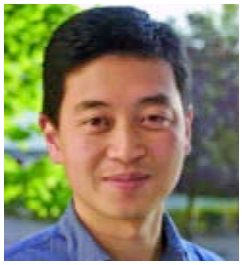

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Conflict of interest
The author declares that there is no conflict of interest as defined by the guidelines of the International Committee of Medical Journal Editors (ICMJE;www.icmje.org).

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CME-Continuing Medical Education

Hypertensive disorders of pregnancy

Question 1
A pregnant woman with a median blood pressure of 150/95 mmHg visits you for the first time in the 24 + 4 week of gestation. The urine dipstick is simple-positive for protein and the patient has no complaints. The findings of the fetal ultrasound are normal. The patient is suffering from
a. hypertension associated with pregnancy,
b. preeclampsia,
c. superimposed preeclampsia,
d. chronic hypertension,
e. none of these diagnoses.

Question 2
The patient should
a. be admitted to hospital immediately and delivery should be induced after lung maturity treatment,
b. be admitted to hospital immediately, and after lung maturity treatment she should undergo antihypertensive treatment with urapidil,
c. should be admitted to hospital immediately, undergo lung maturity treatment and be kept under inpatient surveillance,
d. should not be admitted to hospital, but should receive oral antihypertensive medication (e. g. with alpha-methyldopa)
e. should not be admitted to hospital and not receive any medication, but should be closely monitored as an outpatient.

Question 3
To prevent complications such as the HELLP syndrome, eclampsia, or retardation of fetal growth, the patient should
a. be treated prophylactically with ASS 100 mg/day,
b. be treated prophylactically with dalteparin 2 500 IU/day,
c. be administered ASS 100 mg/day and dalteparin 2 500 IU/day for prophylaxis,
d. receive ASS 100 mg/day and dalteparin 2 500 IU/-day, only if an antiphospholipid-antibody syndrome presents,
e. not be treated prophylactically, as the benefits of such therapy at this stage have not been substantiated.

Question 4
Which of the following is *not* a risk factor for preeclampsia?
a. The patient is over 42 years of age.
b. Rheumatic glomerulonephritis.
c. Pregnancy-associated hypertension in the previous pregnancy.
d. Smoking (20 cigarettes a day).
e. A body mass index of 37.

Question 5
Days after delivery, a 39 year-old I-para undergoes a tonic-clonic seizure on the ward without any apparent cause, in the presence of the nursing staff after spontaneous delivery. The blood pressure is 150/90 mmHg postictal, the urine dipstick findings are normal, as are the laboratory results. After regaining consciousness, the patient says she cannot recall having experienced anything similar before. It was most probably
a. an epileptic attack due to lack of sleep during delivery,
b. an attack of hysterics due to the pressure of the new situation,
c. an eclamptic seizure without any previous preeclamptic symptoms,
d. a transitory ischemic attack due to hypercoagulability,
e. a main side effect following an overdose of oxytocin.

Question 6
The patient in Question 5 should be initially treated with:
a. intravenous diazepam,
b. intravenous magnesium,
c. intravenous phenytoin,
d. intravenous heparin,
e. no medication.

Question 7
A 17 year-old primagravida in the 35th + 1 week of gestation presents at the emergency room complaining of severe pains in the upper abdomen and nausea after eating French fries with mayonnaise. The blood pressure is 140/90 mmHg, the urine dipstick findings are normal and the results of laboratory tests as follows: Hb 13.4 g/dl, leucocytes 12.5/nl, thrombocytes 114/nl, AST 120 U/l, ALT 99 U/l, AP 360 U/l, CRP 2.1 mg/dl. How do you proceed?

a. Repeat the laboratory in two hours. If the thrombocytes have dropped and/or transaminase levels have risen, primary cesarean section should be performed immediately.
b. Repeat the laboratory tests in two hours. If the thrombocytes have dropped and/or transaminase levels have risen, delivery should be induced with prostaglandin.
c. Conservative treatment with infusion therapy and closed-meshed fluid balance.
d. Due to the probability of fetal immaturity, lung maturity treatment should be carried out with 2 x 12 mg betamethasone, and after 48 hours delivery should be induced using prostaglandins.
e. Due to the likelihood of fetal immaturity, lung maturity treatment with 2 x 12 mg betamethasone and after 48 hours primary cesarean section.

Question 8
Which of the following does *not* constitute a risk to the patient after a HELLP syndrome during the present pregnancy?

a. Increased risk of thrombosis of the deep leg veins during confinement.
b. Increased risk of eclampsia during confinement.
c. Increased risk of gestational diabetes in the next pregnancy.
d. Increased risk of preeclampsia in the next pregnancy.
e. Increased risk of chronic hypertension at the age of 60.

Question 9
Which statement is correct?

a. During preeclampsia, the blood pressure rises because the circulating peripheral volumes increase over-proportional to those during normal pregnancy.
b. Proteinuria associated with preeclampsia is a result of increased renal perfusion and the decrease in vascular resistance in the renal arteries.
c. Pathological placental hyperperfusion often develops in preeclampsia due to a centralizing effect in the pregnant woman.
d. In preeclampsia, there is a pathological imbalance between thromboxane and prostacyclin, in favor of thromboxane.
e. The fall in arterial blood pressure during preeclampsia has a favorable hemodynamic effect on the perfusion of the placenta and supply to the fetus.

Question 10
A primagravida with a median blood pressure of 160/95 mmHg consults you in the 38th + 4 week of gestation. She has no complaints; the urine dipstick is simple-positive for protein and the laboratory results are as follows: Hb 11.6 g/dl, leucocytes 9.8/nl, thrombocytes 228/nl, AST 20 U/l, ALT 38 U/l, AP 350 U/l. The sonography shows normal fetal development with a regular amount of amniotic fluid, and the findings of the fetal Doppler are normal. How do you proceed with this patient?

a. Admittance to hospital and immediate primary cesarean section.
b. Admittance to hospital and primary cesarean section when the patient's stomach is empty.
c. Admittance to hospital and induction of labor.
d. Outpatient blood pressure checks and commencement of treatment with alpha-methyldopa.
e. Outpatient checks and induction of delivery at term.